REMARKS

Status of the Claims

Upon entry of these remarks claims 97-100 and 119-127 and 130-152 will be pending. New claims 147-152 have been added. Claims 1-96, 101-118 and 128-129 have been cancelled without prejudice or disclaimer. Applicants reserve the right to file one or more continuing or divisional applications directed to the subject matter of the cancelled claims.

Amendments to the Specification

In accordance with 37 C.F.R. §§ 1.121 and 1.125, Applicants have submitted herewith a substitute specification because the number of amendments required to ensure proper usage of the trademark terms ATCC™ and BLyS™ was so great. Specifically, at page 2 of the Office Action mailed September 14, 2004, in the third paragraph under the heading "Specification," the Examiner has required that the use of trademarks ATCC™ and BLyS™ be capitalized wherever it appears and be accompanied by the generic terminology. In response, Applicants have added the term BLyS™ to paragraphs [0001] and [0002] in the specification. All other instance of "BLyS" in the specification have been amended to B Lymphocyte Stimulator, including in the title. Additionally, each instance of "ATCC" in the specification has been replaced with either "American Type Culture Collection" or ATCC™. Applicants believe these amendments address the Examiner concerns and effect proper usage of these trademarked terms. Applicants submit that no new matter has been added by way of these amendments.

Applicants have also amended paragraphs [0669], [0710] and [0727] to delete the world wide web address (URL) in accordance with the Examiner's requirement (see page 2 of the Office Action mailed September 14, 2004, second paragraph under the heading "Specification"). Applicants have replaced the URL with text that would enable one of skill in the art to locate the website. Applicants submit that no new matter has been added by way of these amendments.

Applicants have also amended Table 1 to correct an obvious error. Specifically, the reported delineation of the amino acid residues that define the light chain variable region (VL region) of certain scFvs in column three of Table 1 were incorrect. An

amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of the error in the specification, but also the appropriate correction. *See*, M.P.E.P. § 2163.07. As detailed in the Declaration Of Rodger Smith Under 37 C.F.R. § 1.132 submitted herewith (hereinafter the "Smith Declaration"), one of ordinary skill in the art would easily have been able to routinely recognize and correct the errors in the third column of Table 1 entitled "AAs of VL".

Briefly, Dr. Smith describes how the specification clearly discloses that the VH and VL regions of the scFvs described in Table 1 and shown in SEQ ID NOS:1-2128 are of human origin. (See paragraph 10 of the Smith Declaration). He explains that light chain VL regions are defined as either kappa or lambda isotypes. (See paragraph 5 of the Smith Declaration). Dr. Smith provides documentary evidence that as of June 16, 2000, the sequences of most, if not all, human VL regions had been determined. (See paragraphs 11-12 of the Smith Declaration). In paragraph 9, Dr. Smith states that "[t]he beginning of the VL region in an scFv may be easily delineated by 1) determining whether the scFv contains a kappa or a lambda variable domain and then 2) calculating the first amino acid sequence based on a standard numbering system for immunoglobulin variable regions that was established by Elvin A. Kabat and Tai Te Wu in the 1970's that is widely used by immunologists even today."

Paragraphs 10-13 of the Smith declaration describe how an antibody scientist on or before June 16, 200 would have been able to identify the VL region in each of the scFvs as either a kappa or lambda VL region. The results of such an analysis for each scFv is further shown in the Table presented as Exhibit E submitted with his declaration. Paragraphs 14 and 15 then further describe that it was known before June 16, 2000 that VL regions have an invariant cysteine residue at what the Kabat-Wu numbering scheme defines as amino acid position 23 in VL regions. He also explains that the Kabat-Wu numbering scheme defines no amino acid number 10 for lambda light chains. Thus, by the Kabat-Wu numbering scheme, there is an invariant cysteine residue at amino acids number 23 of kappa VL regions and amino acid number 22 of lambda VL regions. Dr. Smith states that once the invariant cysteine residue at amino acid number 23 of a kappa VL region or amino acid number 22 of a lambda VL region has been identified, one must simply count backwards to correctly identify the first amino acid of the VL region.

Paragraphs 16-18 of the Smith Declaration explain a little more about the nature of the invariant residue at Kabat Wu position number 23 and the nature of the errors in column 3 in Table 1.

Dr. Smith concludes by stating "[o]n or before June 16, 2000, an antibody scientist examining the sequences described in Table 1 and the Sequence Listing of the '748 patent would have readily recognized that in several instances, the amino acid residues defined in Table 1 as making up the VL region of certain scFvs were incorrect for either containing a few additional amino acids 5' of the VL region or for lacking an amino acid at the 5' end of the VL-region" and that "an antibody scientist would have had no difficulty in identifying the correct amino acid residue that corresponded to the first amino acid residue of the VL region."

Applicants submit that the Smith Declaration demonstrates that the errors in Column 3 of Table 1 were obvious errors as defined by M.P.E.P. § 2163.07 and therefore correction of Table 1 does not constitute new matter.

Applicants also not a typographical error in paragraph [0579] to correct the spelling of "SEQ ID NO:" was effected.

Applicants respectfully request entry of the amendments to the specification described above. Applicants note that only a marked up copy of the specification has been submitted pursuant to The USPTO Official Gazette Notice dated 25 February 2003. Should the Office wish Applicants to also submit a clean copy of the specification, Applicants would be happy to supply it.

Amendments to the Claims

Claims 97 and 100 have been amended to replace the term "BLyS" with the phrase "B Lymphocyte Simulator protein." This amendment is supported by the specification as filed for example at paragraphs [0002] and [0003].

Claims 97 and 100 have also been amended to recite a Markush group identifying B Lymphocyte Simulator proteins by structure. Support for these amendments may be found in the specification as filed, at for example paragraphs [0003], [0012], [0029], [0107], [0108], [0063] and SEQ ID NO:3228.

Claims 97-100 have been amended to recite the corrected VL region of SEQ ID NO: 2 or SEQ ID NO:327, as necessary. This amendment is in accordance with the correction of Table 1 of the Specification as described above.

Claim 100 has been rewritten in independent form.

Claims 130-135 have been amended to delete the term "BLyS" and replace it with the phrase "said protein" which finds antecedent basis ultimately in the phrase "B Lymphocyte Stimulator protein" in claim 97.

New claims 146-152 have been added. Support for new claim 146 may be found in the specification as filed at, for example, [0027], [0273] and [0758]. New claims 147-152 mirror claims 130-135 (as amended), but ultimately depend from claim 100 rather than claim 97. Support for new claims 147-152 may be found in the specification as filed at, for example, in paragraphs [0248]-[0250], [0327]-[0329] and Example 3 (antibodies that neutralize BLyS).

Applicants submit no new matter has been added by way of these amendments and respectfully request entry of these amendments.

Double Patenting Rejections

The Examiner provisionally rejected claims 81 and 82, and 97-145 for either statutory double patenting or double patenting under the judicially created doctrine of obvious-type double patenting over copending U.S. application No. 10/293,418. The Examiner stated that claims 144 and 145 were provisionally rejected under the statutory type double patenting under 35 U.S.C. § 101 (see second full paragraph on page 5 of the Office Action mailed September 14, 2004) and that claims 97-101 and 119-143 were provisionally rejected under the judicially created doctrine of obvious-type double patenting. (see first paragraph on page 6 of the Office Action mailed September 14, 2004). The status of claims 81, 82 and 102-118 was unclear under this rejection, However, Applicants cancellation of these claims herein obviates this rejection at least as it applies to claims 81, 82 and 102-118. Applicants respectfully request that the remaining provisional double patenting rejections be held in abeyance until such time as either the present application or application number 10/293,418 be in condition for allowance but for the double patenting rejections.

Rejections under 35 U.S.C. § 101

Claims 81, 82 and dependent claims 102, 104-108, 111-117 were rejected under 35 U.S.C. § 101 because the claimed invention was allegedly directed to non-statutory subject matter. Without acquiescing to this rejection, in the interest of facilitating the prosecution of this application, Applicants have cancelled claims 81, 82 and dependent claims 102-118, thereby rendering the present rejection moot. Accordingly, Applicants respectfully request that this rejection under 35 U.S.C. § 101 be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 81, 82 and dependent claims 102-118 were rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. Without acquiescing to this rejection, in the interest of facilitating the prosecution of this application, Applicants have cancelled claims 81, 82 and dependent claims 102-118, thereby rendering the present rejection moot. Accordingly, Applicants respectfully request that this rejection under35 U.S.C. § 112, first paragraph be withdrawn.

Claims 97-101 and 119-143 were rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. More specifically, the Examiner maintains that the term "BLyS™ protein" "encompasses a genus of 'B lymphocyte stimulating proteins' which would include species variants of B Lymphocyte Stimulator protein, homomeric and heteromeric multimers of B Lymphocyte Stimulator protein, and proteins not related to SEQ ID NO:3228 that are functionally equivalent (i.e., have B lymphocyte stimulating activity). (See paragraph spanning pages 9-10 of the Office Action mailed September 14, 2004.

Applicants have amended claims 97 and 100 to define B Lymphocyte Stimulator protein as set forth in elements (a) through (c) of claims 97 and 100. Applicants believe these amendments obviate or overcome the rejection. Applicants note for the record, however that the fact that the claimed antibodies specifically bind a B Lymphocyte Stimulator protein as defined in elements (a) through (c) of claims 97 and 100 does not mean that the claimed antibodies may not also bind fragments of the B Lymphocyte Stimulator protein and/or variants of the B Lymphocyte Stimulator protein such as: post-translationally processed forms of the B Lymphocyte Stimulator protein; species

orthologues of B Lymphocyte Stimulator protein; B Lymphocyte Stimulator proteins encoded by alternative alleles or alternatively spliced transcripts; multimers of the B Lymphocyte Stimulator protein that are not trimers of amino acids 134-285 of SEQ ID NO:3228; and/or B Lymphocyte Stimulator fusion proteins or heteromultimers containing a B Lymphocyte Stimulator protein - as long as the antibody binds the B Lymphocyte Stimulator protein portion of said fusion protein or heteromultimer.

In light of the above, Applicants respectfully request that this rejection of claims 97-101 and 119-143 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

Claim 99 was rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. More specifically, the Examiner maintains that recitation of "one or more of the CDR regions" in claim 99 is new matter because the specification at paragraph [0243] to [0244] only teaches that "the percent identity encompass the percent as it relates to any 'one of' the domains listed in Table 1....and not multiples thereof as now claimed." (See paragraph spanning pages 10-11 of the Office Action mailed September 14, 2004).

In response, Applicants direct the Examiners attention to paragraphs [0006], [0015] and [0290] which each indicate that the inventors contemplated antibodies comprising VH and VL domains that differed from the VH and VL domains of the scFvs of SEQ ID NOS 1-2128 in particular regions of the antibodies including in "one or more CDR's". In particular, paragraph [0015] states:

> Antibodies and antibody fragments or variants (including derivatives) of the invention may include, for example, one or more amino acid sequence alterations (addition, deletion, substitution and/or insertion of an amino acid residue). These alterations may be made in one or more framework regions and/or ***one or more CDR's***. (emphasis added)

In view of the foregoing Applicants submit that the recitation of one or more of the CDR regions" in claim 99 is not new matter. Applicants respectfully request that this rejection of claim 99 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

Claims 144 and 145 were rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the enablement requirement. More specifically, the Examiner sates that reference to the Deposits of Biological Material with the American Type Culture Collection (ATCC™) on page 144 of the specification is "an insufficient assurance" that all required deposits have been made and all the conditions of 37 C.F.R. §§ 1.801-1.809 have been met." (See second full paragraph on page 11 of the Office Action mailed September 14, 2004.)

In response, Applicants' representative hereby gives the following assurance by signature below:

Human Genome Sciences, Inc., the assignee of the present application, has deposited biological material under the terms of the Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedure with the following International Depository Authority: American Type Culture Collection (ATCC™), 10801 University Boulevard, Manassas, Virginia 20110-2209. A deposit of the NSO-anti-BLyS-6D08-18 and NSO-anti-BLyS-116A01-60 cell lines was made on March 27, 2001, and given ATCC™ Accession Numbers PTA-3239 and PTA-3240, respectively. In accordance with M.P.E.P. § 2410.01 and 37 C.F.R. § 1.808, assurance is hereby given that all restrictions on the availability to the public of ATCC™ Accession Numbers PTA-3239 and PTA-3240 will be irrevocably removed upon the grant of a patent based on the instant application, except as permitted under 37 C.F.R. § 1.808(b). A partially redacted copy of the ATCC™ Deposit Receipt for Accession Numbers PTA-3239 and PTA-3240 is enclosed herewith.

As a result, Applicants submit that the Examiner's rejection of claims 144-145 under 35 U.S.C. § 112, first paragraph, is obviated by the above statement regarding availability of the deposited material, and Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 81, 82 and 97-145 were rejected under 35 U.S.C. § 112, as allegedly being indefinite. More specifically, the Examiner states that the term "BLyS™ is an active trademark. The use of trademarks is prima facie indefinite because it does any

chemical represented is not inexorably tied to the trademark." (See second full paragraph on page 12 of the Office Action mailed September 14, 2004).

In response, Applicants have removed the term "BLyS" from the claims. In claims 97 and 100, Applicants have amended the term "BLyS" to "B Lymphocyte Stimulator protein" and have provided a set of chemical structures that identify B Lymphocyte Stimulator proteins – at least one of which must be bound by the antibody recited in the claims. Claims 130-135 have been amended to delete the term "BLyS" and replace it with the phrase "said protein" which finds antecedent basis ultimately in the phrase "B Lymphocyte Stimulator protein" in claim 97. In view of the foregoing, Applicants respectfully request that this rejection of claims 81, 82 and 97-145 under 35 U.S.C. § 112, second paragraph be reconsidered and withdrawn.

Claims 81, 82, 144 and 145 were rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. More specifically, the Examiner states that the term "ATCC™" is an active trademark which "should be capitalized wherever it appears and be accompanied by the generic terminology." (See third full paragraph on page 12 of the Office Action mailed September 14, 2004).

In response, Applicants have amended the term "ATCC" to "ATCC™" in claims 144 and 145. As described above, claims 81 and 82 have been cancelled herein. Accordingly, Applicants believe the amendments to claims 144 and 145 obviate or overcome this rejection. Applicants respectfully request that this rejection be reconsidered and withdrawn. In view of the foregoing, Applicants respectfully request that this rejection of Claims 81, 82, 144 and 145 under 35 U.S.C. § 112, second paragraph be reconsidered and withdrawn.

Claims 81 and 82 were rejected under 35 U.S.C. § 112, as allegedly being indefinite for reciting an "antibody that competitively inhibits the binding of the I006D08 [I116A01] antibody...to BLyS, wherein said antibody competitively inhibits said binding more than the I006D08 [I116A01] antibody competitively inhibits itself." Without acquiescing to this rejection, in the interest of facilitating the prosecution of this application, Applicants have cancelled claims 81 and 82 thereby rendering the present

rejection moot. Accordingly, Applicants respectfully request that this rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

Rejections under 35 U.S.C. § 102(b)

Claims 81, 82 and dependent claims 102, 107 and 111-118 were rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Tribouley et al, (1999) *Biological Chemistry* 380:1443-7 or Mukhopadhay et al., (1999) *The Journal of Biological Chemistry* 274:15978-81. Without acquiescing to this rejection, in the interest of facilitating the prosecution of this application, Applicants have cancelled claims 81, 82 and dependent claims 102-118, thereby rendering the present rejection moot. Accordingly, Applicants respectfully request that this rejection under 35 U.S.C. § 102(b) be withdrawn. Applicants also note for the record that "VAF "as recited on page 14 of the Office Action mailed September 14, 2004 is not an alias of B Lymphocyte Stimulator protein; instead applicants believe the Examiner meant "BAFF".

CONCLUSION

Applicants respectfully request that the above remarks be made of record in the file history of the instant application. Applicants respectfully submit that the present application is now in condition for allowance. A Notice of Allowance is earnestly solicited. If in the opinion of the Examiner, a telephone conference would expedite prosecution, the undersigned can be reached at the telephone number indicated below.

If there are any fees due in connection with the filing of this paper, not accounted for on the Fee Transmittal sheet submitted herewith, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 CFR § 1.136 that is not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: December 14, 2004

Michele Shannon

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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Human Genome Sciences, Inc.
Attn: James H. Davis, Esq.
9410 Key West Avenue
Rockville, MD 20850

Deposited on Behalf of: Human Genome Sciences, Inc.

Identification Reference by Depositor:	**Patent Deposit Designation**
Murine NSO myeloma cell line: NSO-anti-BLyS-6D08-18	PTA-3239
Murine NSO myeloma cell line: NSO-anti-BLyS-116A01-60	PTA-3240

The deposits were accompanied by: __ a scientific description _ a proposed taxonomic description indicated above. The deposits were received March 27, 2001 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested April 3, 2001. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Tanya Nunnally, Patent Specialist, Patent Depository

Date: May 7, 2001